

Application No. 09/723,722
Amendment dated October 29, 2003
Reply to Office Action of April 29, 2003

PATENT

REMARKS/ARGUMENTS

Support for the amendment to claim 1 is found at, e.g., page 8, lines 14-19; and, page 4, line 31 to page 5, line 7 of the specification. Support for the amendment to claim 23 is found at, e.g., page 32, lines 30-32. Support for new claim 132 is found at, e.g., page 24, lines 19-24 of the specification. Support for new claim 133 is found at, e.g., page 39, lines 4-5 of the specification.

Restriction/Election

Applicants have elected the polypeptide of SEQ ID NO: 43. The Examiner states that claims 1-4, 18-20, 22-25, and 27-36 read on the elected species. Applicants respectfully point out that claim 15 which is directed to SEQ ID NO 43 also reads on the elected species.

Objections

Specification

Applicant has amended the description of Figure 5, which the Examiner found confusing. The description of SEQ ID 43 as the "proenzyme region" of SEQ ID NO: 2 has been amended to recite, "the active enzyme portion" of SEQ ID NO: 2. Support for this amendment is found at e.g., p. 10, lines 22-24 of the specification.

Claims

As requested by the Examiner, claims 1, 23, and 27 have been amended to correct the improper quotation of the amino acid residues.

Rejections

35 U.S.C. § 112, Second Paragraph

Claims 18-19 and 27-36

Claims 18 and 19, are rejected because they do not further limit claim 1 from which they depend. Claim 1 has been amended to recite "a protein purified to apparent homogeneity comprising a segment of a β -secretase enzyme protein, wherein the segment lacks

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the signal sequence (amino acid residues 1-22 with respect to SEQ ID NO:2) and the putative pro region (amino acid residues 23-45 with respect to SEQ ID NO:2)." Claim 18 further defines the N-terminal and C-terminus of the protein of claim 1. Claim 19 further defines the C-terminus of the protein of claim 19. Thus, the scope of claims 18 and 19 is narrower than the scope of claim 1 from which they depend.

Claims 27-36, are rejected because they do not further limit claim 23 from which they depend. Claim 23 has been amended to recite "a crystalline protein composition formed from the protein of claim 1." Claim 27 further defines the N-terminal and C-terminus of the crystalline protein composition of claim 1. Claim 28 further defines the C-terminus of the protein of claim 27. Claims 29-31 depend from claim 23. Claims 28 and 29 further define the glycosylation state of the crystalline protein composition of claim 23. Claims 32-36 depend from claim 31. Claims 32-36 further define the inhibitor of claim 31. Thus, the scope of claims 27-36 is narrower than the scope of claim 23 from which they depend.

Based on the foregoing, Applicants respectfully request withdrawal of the rejection.

35 U.S.C. § 102

Claims 1-4, 18-19, and 22 are Rejected Under 35 U.S.C. § 102(g) as Allegedly Being Anticipated by Powell (U.S. 6,319,689)

Claims 1-4, 18-19, and 22 are rejected under 35 U.S.C. § 102(g) as allegedly being anticipated by Powell (U.S. 6,319,689). This rejection is respectfully traversed. The disclosure of a U.S. patent publication falls under 102(e) and not 102(g). Applicants respectfully point out to qualify as 102(g) prior art there must be evidence that the subject matter was actually reduced to practice. While the filing of an application for a patent application is a constructive reduction to practice, the filing of an application does not in itself provide the evidence necessary to show an actual reduction to practice of any subject matter disclosed in the application as is necessary to provide a basis for an *ex parte rejection* under 102(g). (See *Cf. In re Zletz*, 13 USPQ 1320, 1323 (Fed. Cir. 1990).

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Anticipation under § 102 requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of Calif.*, 814 F.2d 628, 631 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The "exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference." *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). See also MPEP 2131.

Powell excludes at least one element that is set forth in Applicants' claims 1-4, 18-19, and 22. Claims 1-4, 18-19, and 22 are directed to a protein having a valine at residue 130. Powell does not disclose such an amino acid sequence.

It is the Examiner's position that Powell discloses a beta-secretase enzyme identical to SEQ ID NO: 2 of the instant application. Applicants respectfully point out that the SEQ ID NO: 2 disclosed in the instant application differs from SEQ ID NO: 2 disclosed by Powell at amino acid 130. The instant application discloses a valine residue at position 130, while Powell discloses an glutamic acid residue at position 130. (*See Exhibit 1, attached hereto.*) Applicants note that no sequence alignment was enclosed with the Office Action.

The failure of Powell to teach SEQ ID NO: 2 of the present application precludes an anticipation rejection based on this reference. Therefore, the rejection should be withdrawn.

Claim 20 is Rejected Under 35 U.S.C. § 102(g) as Allegedly Being Anticipated by Gurney (U.S. 6,420,534)

Claim 20 is rejected under 35 U.S.C. § 102(g) as allegedly being anticipated by Gurney (U.S. 6,420,534). This rejection is respectfully traversed. As discussed above, The disclosure of a U.S. patent publication falls under 102(e) and not 102(g). Without agreeing with the basis of this rejection, Applicants have canceled claim 20.

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35 U.S.C. § 103

Claims 23-25 and 27-35 are Rejected Under 35 U.S.C. § 103(a) as Allegedly Being Unpatentable Over Powell in View of the Common Knowledge in Molecular Biology

Claims 23-25 and 27-35 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Powell in view of the common knowledge in molecular biology. The rejection is respectfully traversed.

As discussed above, Powell fails to teach SEQ ID NO: 2 instant application. The citation of Powell further in view of the common knowledge in molecular biology does not establish a *prima facie* case of obviousness. Obviousness requires either that the "references must expressly or impliedly suggest the claimed combination or the Examiner must present a convincing line of reasoning as to why the invention would have been obvious in light of the teachings of the references." *Ex Parte Clapp*, 227 USPQ 972, 973 (BPAI 1985). The Examiner must consider "all of the facts." *In re Lunsford*, 148 USPQ 721, 725 (CCPA 1966). The Examiner is not free to "pick and choose" prior art that supports his position. *Akzo v. US International Trade Commission*, 1 USPQ2d at 1241, 1246 (Fed. Cir. 1986). Obviousness is not established where the prior art as a whole "gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

The Powell reference does not expressly or impliedly suggest the invention of claims 23-25 and 27-36. Claims 23-25 and 27-30 are directed to a crystalline composition of the protein of claim 1. Claims 31-36 are directed to a crystalline composition of the protein of claim 1 further comprising a beta-secretase substrate or inhibitor. It is the position of the Examiner that it would have been obvious to one of ordinary skill in the art to have the composition of beta secretase taught by Powell and modify it by crystallization of the enzyme. The Examiner further states that the probability of success in obtaining the claim invention is 100% because the methods of protein crystallization are routinely used in the art. Applicants respectfully point out that the probability of success in obtaining the claim invention is 0% because Powell fails to

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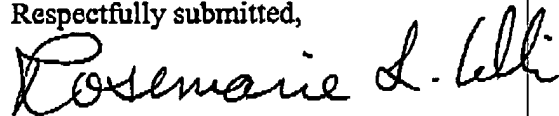
teach SEQ ID No: 2 of the present application. Based on the foregoing, it is respectfully submitted that the rejection should be withdrawn.

Non-statutory double patenting

The claims stand provisionally rejected for obviousness type double patenting over several copending cases. Applicants propose the issues be held in abeyance until indication of allowability in the present case. Applicant will then consider providing a terminal disclaimer over cited cases provided the cited case has been or is about to patented, the claims in the cited case have not been divided from those in the present case by restriction requirement or election of species, and the claims in the cited case are in conflict with those in the present case at this time.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



Rosemarie L. Celli
Reg. No. 42,397

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 650-326-2400
Fax: 650-326-2422
RLC:rlc
60071128 v1

EXHIBIT 1

US Application No. 723,722

<210> 2
 <211> 501
 <212> PRT
 <213> Homo sapiens

<400> 2
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 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255

EXHIBIT 1

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480
 Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
 485 490 495
 Ile Ser Leu Leu Lys
 500

EXHIBIT 1

U.S. 6,319,689

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 501 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(vi) ORIGINAL SOURCE:

(A) ORGANISM: not provided

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2

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Met Ala Gln Ala Leu Pro Trp Leu Leu Trp Met Gly Ala Gly Val
 1           5           10           15
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20           25           30
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35           40           45
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50           55           60
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65           70           75           80
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85           90           95
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
100          105          110
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
115          120          125
Tyr Glu Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
130          135          140
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
145          150          155          160
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165          170          175
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
180          185          190
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
195          200          205
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
210          215          220
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
225          230          235          240
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
245          250          255
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260          265          270
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
275          280          285
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
290          295          300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
305          310          315          320
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
325          330          335

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EXHIBIT 1

Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
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 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480
 Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
 485 490 495
 Ile Ser Leu Leu Lys
 500